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AUTHOR(S):

Nakatsuma, Kenji; Shiomi, Hiroki; Watanabe, Hiroki; Morimoto, Takeshi; Taniguchi, Tomohiko; Toyota, Toshiaki; Furukawa, Yutaka; Nakagawa, Yoshihisa; Horie, Minoru; Kimura, Takeshi

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Comparison of Long-term Mortality After Acute Myocardial Infarction Treated by Percutaneous Coronary Intervention in Patients Living Alone versus Not Living Alone at the Time of Hospitalization

Authors: Kenji Nakatsuma MD[a], Hiroki Shiomi MD[a], Hiroki Watanabe MD[a], Takeshi Morimoto MD/PhD[b], Tomohiko Taniguchi MD[a], Toshiaki Toyota MD[a], Yutaka Furukawa MD[c], Yoshihisa Nakagawa MD[d], Minoru Horie MD[e], Takeshi Kimura MD[a], on behalf of the CREDO-Kyoto AMI investigators

Institutions: [a]Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, 606-8507, Japan, [b]Division of General Medicine, Hyogo College of Medicine, 1-1 Mukogawa-cho, Nishinomiya city, Hyogo, 663-8131, Japan, [c]Division of Cardiology, Kobe City Medical Center General Hospital, Chuo-ku, Kobe city, Hyogo, 650-0046, Japan, [d]Division of Cardiology, Tenri Hospital, 200 Mishima-cho, Tenri city, Nara, 632-8552, Japan, [e]Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu city, Shiga, 520-2192, Japan

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Address for correspondence: Hiroki Shiomi MD,
Department of Cardiovascular Medicine, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, 606-8507, Japan
Telephone number: +81-75-751-4255
Fax number: +81-75-751-3299
E-mail: hishiomi@kuhp.kyoto-u.ac.jp

Abstract

Living alone was reported to be associated with increased risk of cardiovascular disease. There are, however, limited data on the relation between living alone and all-cause mortality in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI). The CREDO-Kyoto AMI registry was a cohort study of patients with AMI enrolled in 26 hospitals in Japan from 2005 through 2007. For the current analysis, we included those patients who underwent PCI within 24 hours of symptom onset and we assessed their living status to determine if living alone would be an independent prognostic risk factor. Among 4109 patients eligible for the current analysis out of 5429 patients enrolled in the CREDO-Kyoto AMI registry, 515 patients (12.5%) were living alone at the time of hospital admission. The cumulative 5-year incidence of all-cause death was 18.3% in the living alone group and 20.1% in the not living alone group (log rank P=0.77). After adjusting for potential confounders, risk of the living alone group relative to the not living alone group for all-cause death was not significantly different (adjusted hazard ratio: 0.82, 95% confidence interval 0.65-1.02; P=0.08). In a subgroup analysis stratified by age, the adjusted risk for all-cause d eath was also not different between the living alone group and the not living alone group both in the older population (>=75 years of age) and the younger population (<75 years of age). In conclusions, living alone was not associated with higher long-term mortality in patients with AMI who underwent PCI.

Key words: Living alone; Acute myocardial infarction.

Introduction

Living alone was reported to be associated with increased risk of cardiovascular disease[1-4] and poorer clinical outcomes after acute myocardial infarction (AMI)[5-10]. However, the proportion of patients who had undergone percutaneous coronary intervention (PCI) was small in these studies. Indeed, some of the recent studies reported no significant association between living alone and mortality after AMI[11, 12]. Therefore, the association between living alone and long-term mortality in patients with AMI undergoing PCI in the current real world clinical practice is controversial. Additionally, living alone in older patients is an important welfare issue in rapidly aging societies. However, little is known about the influence of living alone in older patients on clinical outcomes after AMI. The aim of this study was to determine whether living alone is an independent prognostic risk factor for long-term mortality in patients with AMI who underwent PCI within 24 hours of symptom onset in the real world clinical practice.

Methods

The Coronary REvascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) AMI registry is a physician-initiated non-company-sponsored multicenter registry that enrolled consecutive patients with AMI who underwent coronary revascularization within seven days of the onset of symptoms between January 2005 and December 2007 at 26 tertiary hospitals in Japan (Supplementary Appendix A). The relevant review boards or ethics committees at all 26 participating hospitals approved the study protocol. Obtaining written informed consent from the patients was waived because of the retrospective nature of the study; however, we excluded those patients who refused participation in the study when contacted at follow-up. This strategy is concordant with the guidelines of the Japanese Ministry of Health, Labor and Welfare.

The details on the design and patient enrollment of this registry have been described previously[13]. Among 5429 patients enrolled in this registry, we excluded 9 patients who refused to participate in the study, 195 patients treated by coronary artery bypass grafting (CABG), 689 patients who underwent PCI beyond 24 hours after symptom onset, 30 patients whose symptom onset was unknown, 331 patients for whom the data on living arrangements was not available, and 66 patients who had previous CABG. Therefore, the study population for the current analysis consisted of 4109 patients with AMI who underwent PCI within 24 hours of symptom onset and for whom the data on living arrangements was available (ST segment elevation acute myocardial infarction [STEMI]: n=3615, Non-STEMI: n=494).

Experienced clinical research coordinators from the independent clinical research organization (Research Institute for Production Development, Kyoto, Japan; Supplementary Appendix B) collected baseline clinical, angiographic and procedural characteristics including living arrangement from hospital charts or hospital databases according to pre-specified definitions. Collection of follow-up information was mainly conducted through review of inpatient and outpatient hospital charts by the clinical research coordinators, and additional follow-up information was collected through contact with patients, relatives and/or referring physicians by sending mail with questions regarding vital status, subsequent hospitalizations, and status of antiplatelet therapy. Death, myocardial infarction (MI), and stroke were adjudicated by the clinical event committee (Supplementary Appendix C). Median follow-up duration for the surviving patients was 1844 (inter-quartile range [IQR]: 1508-2163) days. Complete 1- and 3-year follow-up information was obtained in 98.3% and 96.2% of patients, respectively.

We defined living alone as patients who did not live with their family or others at the time of hospital admission. The detailed definitions of baseline clinical characteristics were described previously[13, 14]. The primary outcome measure for the current analysis was all-cause death. The secondary outcome measures included cardiac death, MI, stroke, hospitalization for congestive heart failure, and any coronary revascularization. Death was regarded as cardiac in origin unless obvious non-cardiac causes could be identified. Any death during hospitalization for the index AMI was regarded as cardiac death. MI was defined according to the definition in the Arterial Revascularization Therapy Study[15]. Stroke was defined as ischemic or hemorrhagic stroke either occurring during the index hospitalization or requiring hospitalization with symptoms lasting >24 hours. Hospitalization for congestive heart failure was regarded as present when intravenous drug treatment was required for worsening heart failure. Any coronary revascularization was defined as either PCI or CABG for any reasons. Scheduled staged coronary revascularization procedures performed within 3 months of the initial procedure were not regarded as follow-up events, but were included in the index procedure.

We present continuous variables as mean ± standard deviation or median with IQR and categorical variables as numbers and percentages. We compared categorical variables with the χ^2 test when appropriate; otherwise, we used Fisher's exact test. We compared continuous variables with the Student's t-test or the Wilcoxon rank-sum test on the basis of the distributions.

We used the Kaplan-Meier method to estimate cumulative incidences of clinical event rates and assessed differences with the log-rank test. The effects of the living alone group relative to the not living alone group for individual endpoints were expressed as hazard ratios (HR) with 95% confidence intervals (CI) by

multivariable Cox proportional hazard models adjusting for the 40 clinically relevant factors indicated in Table 1, 2 and 3. Consistent with our previous reports, continuous variables were dichotomized using clinically meaningful reference values or median values. A subgroup analysis stratified by patients' age (>= 75 years old or < 75 years old) was also conducted. Statistical analyses were conducted using JMP 10.0 (SAS Institute Inc., Cary, North Carolina). All the statistical analyses were 2-tailed. We regarded P values <0.05 as statistically significant.

Results

Regarding the baseline clinical characteristics, the living alone group had significantly higher prevalence of patients with advanced age, female gender, history of heart failure, and liver cirrhosis (Table 1). The living alone group also had a significantly longer onset-to-presentation time compared with the not living alone group (Figure 1). However, there was no significant difference in the angiographic and procedural characteristics between the 2 groups except for the lower prevalence of multivessel coronary artery disease in the living alone group. Regarding medical treatment at discharge, beta-blockers were more often prescribed in the living alone group (Table 2 and 3).

The cumulative incidence of all-cause death was not significantly different between the living alone and not living alone groups at 5 years (Figure 2A). After adjustment for potential confounding factors, the risk for all-cause death in the living alone group remained to be comparable with that in the not living alone group. The unadjusted and adjusted risk for cardiac death, MI, stroke, and any coronary revascularization were also not different between the 2 groups (Figure 2B, Supplemental Figure 1A, 1B and 1D). However, the cumulative incidence of readmission for heart failure in the living alone group was significantly higher than that in the not

living alone group, although the adjusted risk of the living alone group relative to the not living alone group for readmission for heart failure was not statistically significant (Supplemental Figure 1C and Table 4).

In the population of patients with <75 years of age, the cumulative 5-year incidence of all-cause death was not different between the living alone and the not living alone group. The cumulative incidence of all the other clinical endpoints were also not different between the 2 groups in the subgroup of patients with <75 years of age (Table 4). On the other hand, the cumulative 5-year incidence of all-cause death and cardiac death in the living alone group were significantly lower than those in the not living alone group in the subgroup of patients with >=75 years of age. However, after adjusting the confounders, lower risk of the living alone group relative to the not living alone group for all-cause death was no longer significant in the subgroup of patients with >=75 years of age, although the adjusted risk for cardiac death in the living alone group remained significant. Regarding the other clinical endpoints, the adjusted outcomes between the living alone group and the not living alone group were not significantly different in the subgroup of patients with >=75 years of age (Table 4).

Discussion

The main findings in this study were as follows; (1) Living alone was not associated with higher long-term mortality in patients with AMI who underwent PCI within 24 hours of symptom onset; (2) The risk for readmission for heart failure was also not significantly different between the living alone group and the not living alone group; (3) These results were consistently observed regardless of patients' age.

Living alone in older patients is an important welfare issue in the rapidly aging societies. The Statistics Bureau of Japan reported that percentage of people living alone in Japan was 11.3% in 2005 and 13.1%

in 2010 (12.5% in the current study)[16]. However, little is known about the influence of living alone in older patients on the clinical outcome after AMI. In previous studies, living alone was reported to be associated with increased risk of cardiovascular disease[1-4] and poorer clinical outcomes after AMI[5-10]. However, most studies enrolled not only patients receiving primary PCI but also those with lytic therapy or those not receiving reperfusion therapy. Moreover, some of recent studies reported no significant association between living alone and mortality after AMI[11, 12]. Therefore, the association between living alone and long-term mortality after AMI in patients with PCI is controversial in the current real world clinical practice.

In contrast to many previous reports, living alone was not associated with higher long-term mortality in patients with AMI who underwent PCI within 24 hours of symptom onset in the current study. One of the possible reasons for this discrepancy might be the difference in the baseline characteristics of the enrolled patients. The average of patients' age in the current study was much higher than those in other studies, and all the patients in the current study received PCI in the AMI setting. In older population, patients living alone might be more likely to have good functional status, which has been reported to be a powerful predictor of survival in older people[17-19]. Another possible reason for the discrepancy between the current and previous studies might be the health insurance system in Japan, where public health insurance system covers everyone. Previous studies reported that patients living alone tended to have a higher unemployment rate and lower incomes[3, 8, 11, 20], and other studies also reported that lower-income patients were less likely to receive primary PCI[21, 22]. Indeed, the recent study evaluating living arrangement and mortality after AMI in Japan also reported no significant difference in long-term mortality between the living alone and not living alone patients[23].

As mentioned before, older patients living alone might be more likely to have good functional

status, which was a powerful predictor of survival in older people. On the other hand, patients living alone might have difficulties in receiving social support. These two factors might have directionally opposite impact on the relation between living arrangement and clinical outcome after AMI[19]. Furthermore, The current study as well as previous studies could not evaluate the patients living alone who suffered from AMI and died before hospital arrival. Indeed, the time from symptom onset to arrival to the hospital was much longer in patients living alone than those in patients not living alone in the current study. Total ischemic time was reported to be an important factor associated with long-term mortality in patients with STEMI undergoing primary PCI[13]. In this point of view, it would be important to reinforce the social welfare system to support the living alone patients in emerging setting.

This study has several limitations. First, observational study design precluded definitive conclusions because of selection bias and unmeasured confounders. Second, we did not collect data on the changes in living arrangements after discharge from the index hospitalization, as well as functional, psychological, educational, and socioeconomic status, although those factors might be powerful predictors for mortality after AMI. Therefore, future well-conducted prospective studies in which those data are corrected will be desired. Third, practice style in Japan, such as longer length of hospital stay after AMI, is different from those outside Japan[24]. Finally, patient demographics and clinical outcomes in AMI patients with living alone in Japan may be also different from those outside Japan. Therefore, generalizing these results to populations outside Japan should be done with caution.

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Legends to Figures

Figure 1. Onset to presentation time and door to balloon time according to living arrangements.

Figure 2. Clinical outcomes according to living arrangements. Cumulative incidences of all-cause death (A) and cardiac death (B) were compared between the living alone group and not living alone group.

Table 1. Baseline clinical characteristics according to living arrangements

	Living alone	Not living alone	P value
Variable	(n = 515)	(n = 3594)	
Age (years)	68.5 ± 13.0	67.6 ± 12.1	0.11
Age >=75 years*	196 (38%)	1097 (31%)	0.001
Men*	322 (63%)	2701 (75%)	<0.001
Body mass index (kg/m^2) <25.0*	390 (76%)	2586 (72%)	0.07
Hypertension*	407 (79%)	2826 (79%)	0.84
Diabetes mellitus	159 (31%)	1157 (32%)	0.55
on insulin therapy*	19 (3.7%)	160 (4.5%)	0.43
Current smoker*	206 (40%)	1430 (40%)	0.93
Heart failure*	188 (37%)	1093 (30%)	0.005
Multivessel coronary disease*	243 (47%)	1884 (52%)	0.03
Mitral regurgitation grade 3/4*	13 (2.5%)	115 (3.2%)	0.41
Prior myocardial infarction*	44 (8.5%)	307 (8.5%)	0.99
Prior percutaneous coronary intervention*	40 (7.8%)	316 (8.8%)	0.44
Prior stroke (symptomatic)*	50 (9.7%)	331 (9.2%)	0.72
Peripheral vascular disease*	17 (3.3%)	119 (3.3%)	0.99
eGFR (ml/min/1.73 m^2) < 30, without hemodialysis*	27 (5.2%)	150 (4.2%)	0.26
Hemodialysis*	11 (2.1%)	52 (1.5%)	0.23
Atrial fibrillation*	53 (10%)	333 (9.3%)	0.46
Anemia (Hemoglobin <11.0 g/dl)*	62 (12%)	338 (9.4%)	0.06
Thrombocytopenia (Platelet count <100,000)*	11 (2.1%)	65 (1.8%)	0.61
Chronic obstructive pulmonary disease*	23 (4.5%)	113 (3.1%)	0.12
Liver cirrhosis*	20 (3.9%)	76 (2.1%)	0.02
Malignancy*	34 (6.6%)	293 (8.2%)	0.22

Categorical variables are expressed as number (%) unless otherwise indicated. Continuous variables are shown as mean ± SD or median (interquartile range).

* Potential independent variables selected for Cox proportional hazard models. SD = standard deviation; eGFR = estimated glomerular filtration rate.

Table 2. Presentation and Angiographic characteristics according to living arrangements

	Living alone	Not living alone	P value
Variable	(n = 515)	(n = 3594)	
ST-segment elevation myocardial infarction	453 (88%)	3162 (88%)	0.99
Hours from onset to presentation	3.1 (1.3-6.4)	2.4 (1.2-5.3)	0.001
<=2 hours	189 (39%)	1541 (45%)	0.01
Minutes from door to balloon	90 (60-138)	96 (66-138)	0.16
Hemodynamics:			
Killip class 1	365 (71%)	2682 (75%)	0.04
Killip class 2	59 (11%)	279 (7.8%)	
Killip class 3	14 (2.7%)	105 (2.9%)	
Killip class 4*	77 (15%)	528 (15%)	
Duration of hospitalization (days)	15 (10-22)	15 (10-23)	0.06
Infarct related coronary artery			
Left anterior descending	249 (48%)	1602 (45%)	0.32
Left circumflex	69 (13%)	471 (13%)	
Right	180 (35%)	1419 (40%)	
Left main	13 (2.5%)	85 (2.4%)	
Number of target coronary narrowings	1 (1-2)	1 (1-2)	0.76
Target of proximal Left anterior descending coronary artery*	286 (56%)	1909 (53%)	0.30
Target of unprotected Left main coronary artery*	19 (3.7%)	131 (3.6%)	0.96
Target of chronic total occlusion*	17 (3.3%)	122 (3.4%)	0.91
Target of bifurcation*	146 (28%)	956 (27%)	0.40
Side-branch stenting*	14 (2.7%)	122 (3.4%)	0.42
Total number of stents	1 (1-2)	1 (1-2)	0.97
Total stent length >28mm*	207 (44%)	1422 (43%)	0.79
Minimum stent size <3.0mm*	175 (37%)	1105 (34%)	0.13
Drug eluting stent use (culprit or other lesions)*	151 (32%)	1092 (33%)	0.60

Categorical variables are expressed as number (%) unless otherwise indicated. Continuous variables are shown as mean ± SD or median (interquartile range).

* Potential independent variables selected for Cox proportional hazard models. SD = standard deviation.

Table 3. Medications at discharge according to living arrangements

	Living alone	Not living alone	P value
Variable	(n = 515)	(n = 3594)	
Antiplatelet therapy			
Thienopyridine	495 (96%)	3427 (95%)	0.44
Ticlopidine	443 (90%)	3164 (92%)	0.03
Clopidogrel	51 (10%)	259 (7.6%)	0.03
Aspirin	508 (99%)	3545 (99%)	0.99
Cilostazol*	158 (31%)	1266 (35%)	0.04
Other medications			
Statins*	260 (50%)	1930 (54%)	0.17
Beta-blockers*	238 (46%)	1465 (41%)	0.02
ACE-I/ARB*	368 (71%)	2622 (73%)	0.47
Nitrates*	168 (33%)	1081 (30%)	0.24
Calcium channel blockers*	103 (20%)	769 (21%)	0.47
Nicorandil*	148 (29%)	1002 (28%)	0.69
Warfarin*	45 (8.7%)	385 (11%)	0.17
Proton pump inhibitors*	185 (36%)	1259 (35%)	0.69
H2-blockers*	167 (32%)	1155 (32%)	0.90

Categorical variables are expressed as number (%) unless otherwise indicated. Continuous variables are shown as mean ± SD or median (interquartile range).

* Potential independent variables selected for Cox proportional hazard models. SD = standard deviation;

ACE-I = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers.

Table 4. Clinical outcomes in patients living alone compared with patients not living alone

Variable	Living alone	Not living alone	Unadjusted			Adjusted		
	N of patients with events (Cumulative incidence)	N of patients with events (Cumulative incidence)	Living alone		P value	Living alone		P value
			HR	95% CI		HR	95% CI	
	(n = 515)	**(n = 3594)**						
All-cause death	87 (18%)	693 (20%)	0.97	(0.79-1.19)	0.77	0.82	(0.65-1.02)	0.08
Cardiac death	49 (10%)	405 (12%)	0.94	(0.70-1.23)	0.65	0.78	(0.57-1.04)	0.10
Myocardial infarction	26(6.0%)	167 (5.3%)	1.11	(0.73-1.62)	0.62	0.99	(0.63-1.48)	0.95
Stroke	27 (6.0%)	204 (6.5%)	0.94	(0.62-1.35)	0.73	0.96	(0.63-1.41)	0.82
Readmission for heart failure	59 (14%)	262 (8.4%)	1.55	(1.16-2.04)	0.004	1.22	(0.88-1.65)	0.22
Any coronary revascularization	173 (38%)	1204 (38%)	1.00	(0.86-1.17)	0.99	1.11	(0.93-1.30)	0.24
Patients <75 years of age	**(n = 319)**	**(n = 2497)**						
All-cause death	33 (11%)	255 (11%)	1.11	(0.79-1.53)	0.53	0.75	(0.50-1.09)	0.13
Cardiac death	22 (7.2%)	156 (6.4%)	1.23	(0.80-1.82)	0.34	0.91	(0.55-1.43)	0.68
Myocardial infarction	13 (4.7%)	102 (4.4%)	1.07	(0.60-1.77)	0.81	1.05	(0.57-1.79)	0.88
Stroke	12 (4.2%)	108 (4.7%)	0.69	(0.48-1.52)	0.69	0.92	(0.48-1.61)	0.78
Readmission for heart failure	21 (7.2%)	111 (4.9%)	1.44	(0.88-2.23)	0.14	1.01	(0.59-1.66)	0.96
Any coronary revascularization	119 (41%)	918 (39%)	0.80	(0.84-1.23)	0.80	1.12	(0.91-1.36)	0.28
Patients >=75 years of age	**(n = 196)**	**(n = 1097)**						
All-cause death	54 (30%)	438 (42%)	0.71	(0.54-0.92)	0.009	0.79	(0.59-1.04)	0.10
Cardiac death	27 (16%)	249 (25%)	0.64	(0.43-0.91)	0.01	0.65	(0.42-0.97)	0.04
Myocardial infarction	13 (8.2%)	65 (8.0%)	1.04	(0.55-1.82)	0.89	0.87	(0.43-1.62)	0.67
Stroke	15 (9.3%)	96 (12%)	0.82	(0.47-1.35)	0.45	0.96	(0.53-1.63)	0.87
Readmission for heart failure	38 (26%)	151 (18%)	1.32	(0.92-1.86)	0.13	1.29	(0.84-1.92)	0.24
Any coronary revascularization	54 (33%)	286 (33%)	1.00	(0.74-1.33)	0.98	1.12	(0.80-1.53)	0.49

Cumulative incidence was estimated by the Kaplan-Meier method.

Unadjusted and adjusted HR and 95% CI were estimated by the Cox proportional hazard models. HR = hazard ratio; CI = confidence interval.

Figure 1

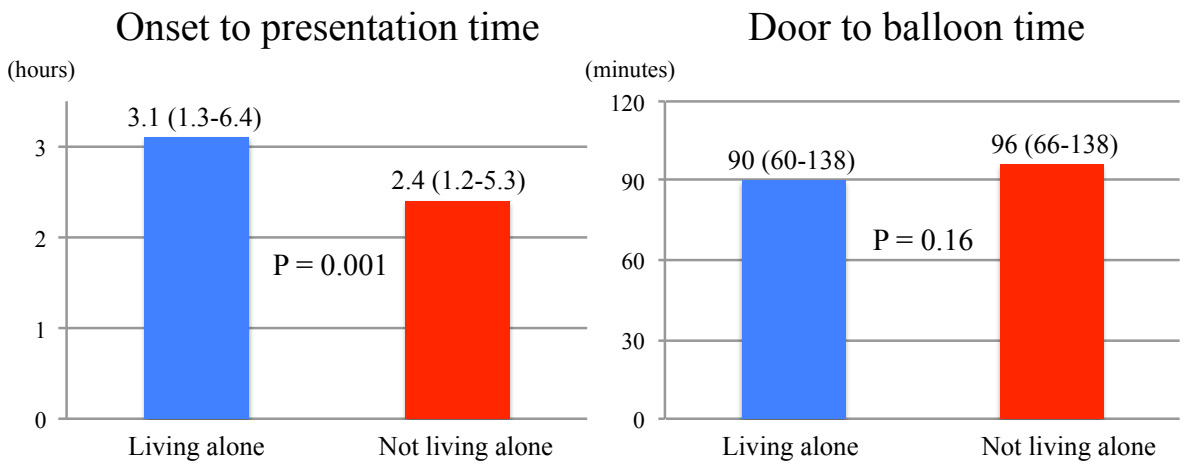
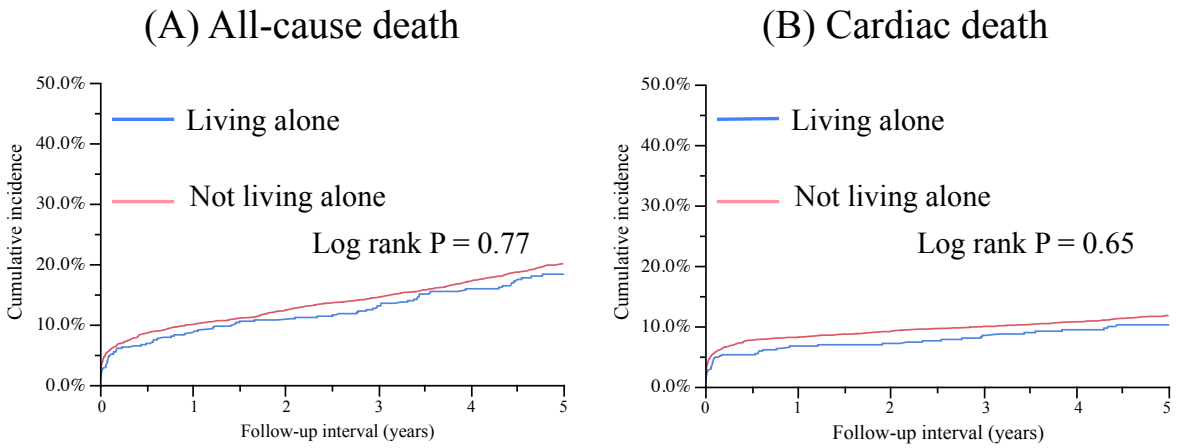


Figure 2



Interval	0 days	30 days	1 year	3 years	5 years
Living alone					
N of events		21	44	65	87
N of patients at risk	515	490	449	406	251
Cumulative incidence		4.1 %	8.7 %	13.1 %	18.3 %
Not Living alone					
N of events		198	358	516	693
N of patients at risk	3594	3384	3190	2967	1880
Cumulative incidence		5.5 %	10.0 %	14.5 %	20.1 %

Interval	0 days	30 days	1 year	3 years	5 years
Living alone					
N of events		21	34	42	49
N of patients at risk	515	490	449	406	251
Cumulative incidence		4.1 %	6.7 %	8.5 %	10.2 %
Not Living alone					
N of events		194	292	353	405
N of patients at risk	3594	3384	3190	2967	1880
Cumulative incidence		5.4 %	8.2 %	10.0 %	11.8 %